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## **Serial lactate and admission SOFA scores in trauma: an analysis of predictive value in 724 patients with and without traumatic brain injury**

Dübendorfer, C ; Billeter, A T ; Seifert, Burkhardt ; Keel, M ; Turina, M

**Abstract:** Objective Arterial lactate, base excess (BE), lactate clearance, and Sequential Organ Failure Assessment (SOFA) score have been shown to correlate with outcome in severely injured patients. The goal of the present study was to separately assess their predictive value in patients suffering from traumatic brain injury (TBI) as opposed to patients suffering from injuries not related to the brain. **Materials and methods** A total of 724 adult trauma patients with an Injury Severity Score (ISS)  $\geq 16$  were grouped into patients without TBI (non-TBI), patients with isolated TBI (isolated TBI), and patients with a combination of TBI and non-TBI injuries (combined injuries). The predictive value of the above parameters was then analyzed using both uni- and multivariate analyses. **Results** The mean age of the patients was 39 years (77 % males), with a mean ISS of 32 (range 16–75). Mortality ranged from 14 % (non-TBI) to 24 % (combined injuries). Admission and serial lactate/BE values were higher in non-survivors of all groups (all  $p < 0.01$ ), but not in patients with isolated TBI. Admission SOFA scores were highest in non-survivors of all groups ( $p = 0.023$ ); subsequently septic patients also showed elevated SOFA scores ( $p < 0.01$ ), except those with isolated TBI. In this group, SOFA score was the only parameter which showed significant differences between survivors and non-survivors. Receiver operating characteristic (ROC) analysis revealed lactate to be the best overall predictor for increased mortality and further septic complications, irrespective of the leading injury. **Conclusion** Lactate showed the best performance in predicting sepsis or death in all trauma patients except those with isolated TBI, and the differences were greatest in patients with substantial bleeding. Following isolated TBI, SOFA score was the only parameter which could differentiate survivors from non-survivors on admission, although the SOFA score, too, was not an independent predictor of death following multivariate analysis.

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# Serial lactate and admission SOFA scores in trauma: an analysis of predictive value in 724 patients with and without traumatic brain injury

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## Abstract

**Objective** Arterial lactate, base excess (BE), lactate clearance, and Sequential Organ Failure Assessment (SOFA) score have been shown to correlate with outcome in severely injured patients. The goal of the present study was to separately assess their predictive value in patients suffering from traumatic brain injury (TBI) as opposed to patients suffering from injuries not related to the brain.

**Materials and methods** A total of 724 adult trauma patients with an Injury Severity Score (ISS)  $\geq 16$  were grouped into patients without TBI (non-TBI), patients

with isolated TBI (isolated TBI), and patients with a combination of TBI and non-TBI injuries (combined injuries). The predictive value of the above parameters was then analyzed using both uni- and multivariate analyses.

**Results** The mean age of the patients was 39 years (77 % males), with a mean ISS of 32 (range 16–75). Mortality ranged from 14 % (non-TBI) to 24 % (combined injuries). Admission and serial lactate/BE values were higher in non-survivors of all groups (all  $p < 0.01$ ), but not in patients with isolated TBI. Admission SOFA scores were highest in non-survivors of all groups ( $p = 0.023$ ); subsequently septic patients also showed elevated SOFA scores ( $p < 0.01$ ), except those with isolated TBI. In this group, SOFA score was the only parameter which showed significant differences between survivors and non-survivors. Receiver operating characteristic (ROC) analysis revealed lactate to be the best overall predictor for increased mortality and further septic complications, irrespective of the leading injury.

**Conclusion** Lactate showed the best performance in predicting sepsis or death in all trauma patients except those with isolated TBI, and the differences were greatest in patients with substantial bleeding. Following isolated TBI, SOFA score was the only parameter which could differentiate survivors from non-survivors on admission, although the SOFA score, too, was not an independent predictor of death following multivariate analysis.

**Keywords** Trauma · Infection · Sepsis · Lactate · Base excess · SOFA score

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## Introduction

Severely injured patients are difficult to assess with respect to their individual risk of developing both septic and

non-septic complications, which may lead to organ dysfunction and, ultimately, failure. Several prognostic parameters have been studied, which should aid clinicians in identifying patients in need of early prophylactic or therapeutic interventions. Lactate as a product of undesired anaerobic metabolism has been described as a predictive parameter for mortality and rate of multiple organ failure (MOF) in trauma patients early on [1]. Lactate is also used as a parameter by which to judge the quality of the initial resuscitation, either as a finite value or as the time needed until a defined lactate threshold value has been undercut, a method usually referred to as lactate clearance. Abramson et al. [2], in 1993, showed significantly higher mortality in trauma patients in whom lactate values did not clear to the physiologic range within 24 h after intensive care unit (ICU) admission. Other authors have shown improved outcome in septic patients with early lactate clearance [3]. Furthermore, elevated lactate upon admission has been shown to serve as a risk factor for mortality due to MOF in subsequently septic patients independent of previous signs of multiple organ dysfunction syndrome (MODS) [4]. However, despite the widespread use of lactate as an endpoint for resuscitation in critically ill patients and as marker for risk stratification, previous studies failed to show a true survival benefit in lactate-directed treatment [5].

Base excess (BE), or base deficit, is also widely used in clinical practice as a marker of acid–base regulation. Davis et al. showed that negative BE is a marker for ongoing hemorrhage in multiply injured patients and should be used as guide for volume therapy [6]. Before the introduction of blood gas analyzers capable of rapid lactate measurements ('point of care testing'), BE was used as a surrogate parameter, as it is believed to be mainly driven by lactate elevations in trauma patients [7].

However, the inadequacy of any single parameter to reliably predict outcome is obvious from a physiologic point of view, and a number of scores have been developed in order to provide a more complete picture of the underlying physiologic derangement. The Sequential Organ Failure Assessment (SOFA) score, primarily called the Sepsis-related Organ Failure Assessment, was developed by Vincent et al. [8] in Belgium in the mid 1990s with the goal of predicting outcome in septic patients. A large study conducted from a prospective database in surgical and medical intensive care patients revealed the value of this score in predicting MOF independent of the underlying disease [9]. Later, the score was adapted to subgroups of ICU patients, such as trauma and cancer patients, with a persistently good accuracy in predicting MOF [10, 11].

Unfortunately, most existing studies on predictive parameters in trauma patients were conducted in heterogeneous study populations. By nature, trauma patients differ heavily with respect to injury patterns and

subsequent clinical course, making specific multivariate analyses on prognostic parameters difficult to conduct; while it is clear that patients suffering from isolated head injuries show different systemic reactions to the initial resuscitation than patients with hemorrhagic shock, it suggests, itself, that the above listed parameters show different patterns in trauma patient subsets. The goal of the present study was to define the predictive value of arterial lactate, BE, lactate clearance, Glasgow Coma Scale (GCS) score, and SOFA score for death and sepsis in different subgroups of trauma patients, depending on the presence or absence of traumatic brain injury (TBI).

## Patients and methods

### Patient collective

We have retrospectively analyzed our tertiary referral trauma center's database, including all patients admitted between January 1, 1996 and December 31, 2006 who met the inclusion criteria as defined below. In this timeframe, detailed data on serial lactate, BE, and SOFA scores are available. All patients were treated according to Advanced Trauma Life Support (ATLS) guidelines. Hemodynamically stable patients underwent whole-body computed tomography (CT), whereas immediate surgery was performed in hemodynamically unstable patients ahead of further diagnostic measures.

Inclusion criteria were an Injury Severity Score (ISS) of 16 or greater in patients  $\geq 16$  years of age. Patients with burn injuries, secondary referrals, and patients who received comfort care only due to the severity of their injuries were excluded from further analysis. Early deaths were not excluded. Seventy patients died during the first 48 h after admission, resulting in 654 patients alive at hospital day 3. In total, 724 of 1,537 trauma room admissions were successfully enrolled and divided into the following groups. The first group consisted of patients without significant TBI (referred to as the non-TBI group). No significant head injury was defined as Abbreviated Injury Scale (AIS) head/neck  $\leq 2$ . The second group comprised patients suffering from isolated head injury (AIS  $\geq 3$ , the isolated TBI group). The third group consisted of patients with significant injuries to the head and at least one other anatomic site (combined injury group). Again, each single AIS has to be  $\geq 3$ .

### Definitions of systemic inflammatory syndrome and sepsis

Systemic inflammatory response syndrome (SIRS) and sepsis were defined as recommended by the Consensus

Conference Committee of the American College of Chest Physicians/Society of Critical Care Medicine [12]. Sepsis was diagnosed when at least two SIRS criteria were fulfilled and positive blood cultures were obtained.

#### Laboratory measurements

The time points for serial measurements of arterial lactate and BE were admission to the trauma room, and 1, 2, 3, 4, 6, 8, 12, 24, and 48 h after admission. Lactate clearance was defined as the relative change of arterial lactate within 24 h according to our earlier work by using four different groups [13]: group 1 with lactate values always below 2.5 mmol/L, group 2 with decreasing lactate values from above 2.5 to below 2.5 mmol/L, group 3 with increasing lactate values from below 2.5 to above 2.5 mmol/L, and group 4 with values always above 2.5 mmol/L at 24 h after admission. All blood samples were analyzed using a standard radiometer for blood gas analysis (ABL800 FLEX; Drott Medizintechnik, Wien Neudorf, Austria).

#### Organ failure score calculation

The SOFA score was calculated on the admission day and every following day according to Vincent et al. [8]. Finally, the highest value during hospitalization was recorded. Organ dysfunction was defined as a SOFA score  $\geq 5$ .

#### Glasgow Coma Scale

We used the first GCS score assessed by paramedics or an emergency physician at the scene of the accident. We decided to use this value because the hospital admission GCS score is often lower due to the use of analgesics and sedative agents and because of the fact that patients with assumed brain injury often arrive intubated and mechanically ventilated.

#### Statistical analysis

Lactate values were logarithmically transformed, and BE and SOFA scores were used without transformation. Lactate clearance groups were used as outlined above. We performed an exploratory analysis using the Mann–Whitney *U*-test to detect significant differences between the groups regarding the length of mechanical ventilation, length of ICU stay, and length of hospital stay. In nominal parameters such as death, sepsis, and infections, we used Pearson's Chi-square test. Subsequently, the physiologic parameters (lactate, BE, and lactate clearance) and admission SOFA score as well as accident GCS score were analyzed using receiver operating characteristic (ROC) curves. The data were then analyzed using a stepwise

logistic regression analysis to determine whether two parameters together show superior prediction of outcome than one parameter alone. A total of 358 patients were included in the logistic regression, which included the following parameters: gender, age, ISS, New Injury Severity Score (NISS), GCS score at admission, SOFA score at admission, and absolute lactate and BE values until 8 h after admission.

The data are presented as mean (range), mean  $\pm$  standard error of the mean (SEM), or 95 % confidence interval (CI), as appropriate. Statistical significance was defined at  $p < 0.05$ . Statistical analyses were performed using SPSS 18.0 software (IBM SPSS Inc., Chicago, IL, USA) and visualizations were made using SigmaPlot 11.0 (Systat Software, Richmond, CA, USA).

## Results

### Overview of the patient collective

An overview of the patients enrolled into this study and the subgroups used is shown in Table 1. The mean patient age across all groups was 39 years, and 77 % of patients were male. The majority of patients suffered from blunt trauma (90 %). Motor vehicle accidents (MVAs) accounted for the majority of injuries, with the highest rate observed in the combined injury group (70 %) and the lowest in isolated TBI (38 %). In isolated TBI, falls from low heights contributed to 40 % of patients. The ISS ranged from 23 in isolated TBI patients to 37 in the combined injury group. With respect to the injury severity of different body regions, there were no differences in AIS head/neck between isolated TBI and combined injury patients ( $4.36 \pm 0.75$  vs.  $4.35 \pm 0.72$ ). Also, there was no difference with respect to AIS thorax, abdomen, and extremities between the combined injury and the non-TBI patients. Admission Acute Physiology and Chronic Health Evaluation II (APACHE II) score was highest in patients with combined injuries and lowest in non-TBI patients (Table 1). Patients with a subsequently septic or fatal course showed no significantly different admission APACHE II values. The overall mortality was 19 %, with the lowest mortality in patients without TBI (13.6 %) and the highest in the combined injury group, with almost 24 %. Surprisingly, in the entire collective, non-survivors have a significantly lower ISS than survivors ( $29.2 \pm 0.9$  in non-survivors vs.  $32.6 \pm 0.5$  in survivors,  $p = 0.009$ ). This was due to a high percentage of fatal but isolated head injuries, for which our hospital serves as a referral center. Sepsis was diagnosed, on average, on day 8, with 20.0 % of patients becoming septic at some point. The main septic foci were ventilator-associated pneumonia (68.8 % of sepsis cases) and central line

**Table 1** Overview of the patient collective enrolled

	All patients	Non-TBI	Isolated TBI	Combined injuries	<i>p</i> -value
Number of patients	724	301	129	294	
Age (years)	39 (16–86)	40.6 (16–86)	42.3 (16–80)	35.9 (16–86)	0.001
Gender: male (%)	77	77	79	77	n.s.
Blunt trauma (%)	90	80.1	94.6	97.6	<0.001
Type of injury (%)					
MVA	54.7	46.5	38	70.4	<0.001
Work	13	12.6	16.3	11.9	n.s.
Suicide	8.1	11.6	5.4	5.8	0.002
Others	24.2	29.3	40.3	11.9	<0.001
Injury Severity Score	31.9 (16–75)	30.3 (16–66)	23.8 (16–75)	37.2 (17–75)	<0.001
Admission parameters					
MAP admission (mmHg)	90.1 (30–150)	87.6 (35–140)	97.4 (35–150)	80 (30–150)	n.s.
GCS score accident scene	9.8 (3–15)	12.9 (3–15)	7.9 (3–15)	7.5 (3–15)	<0.001
Lactate admission (mmol/L)	3.6 (0.4–20.1)	3.9 (0.7–20.1)	2.8 (0.4–15.5)	3.6 (0.6–19)	<0.001
BE admission (mmol/L)	−5 (−34.9–21)	−5.9 (−29.9–6.7)	−2.3 (−16.8–4.2)	−5.3 (−35–21)	<0.001
SOFA score admission	7 (0–16)	5.9 (0–16)	7.1 (0–15)	8 (0–16)	<0.001
APACHE II score admission	15.9 (0–44)	13.9 (0–38)	15.6 (2–32)	18.1 (0–44)	<0.001
Course of hospital stay					
Length of hospital stay (days)	22.5 (1–167)	24.5 (1–167)	18.1 (1–62)	22.5 (1–101)	0.01
Length of ICU stay (days)	12 (0–101)	8.7 (0–51)	13.2 (0–58)	14.8 (0–101)	<0.001
Length of mechanical ventilation (days)	7.8 (0–101)	4.3 (0–30)	9.7 (0–43)	10.4 (0–101)	<0.001
Mortality (%)	19	13.6	19.4	23.8	n.s.
Head injury	8.4	0	14	14.3	<0.001
Shock	5.4	8.6	0	4.4	0.003
MOF	5.1	5	5.4	5.1	n.s.

Data are listed as mean (range) or as stated in the table

Lactate admission refers to the first arterial lactate value obtained in the trauma room, usually during the initial phase of resuscitation

MAP mean arterial pressure, GCS Glasgow Coma Scale, SOFA Sequential Organ Failure Assessment, APACHE II Acute Physiology and Chronic Health Evaluation II, ICU intensive care unit, MVA motor vehicle accident, BE base excess, MOF multiple organ failure

infections (28.6 %). Interestingly, the rate of fatal MOF was similar in all three groups (5 %). There was no difference in the rate of shock at admission, defined as systolic blood pressure  $\leq 90$  mmHg, among the three subgroups.

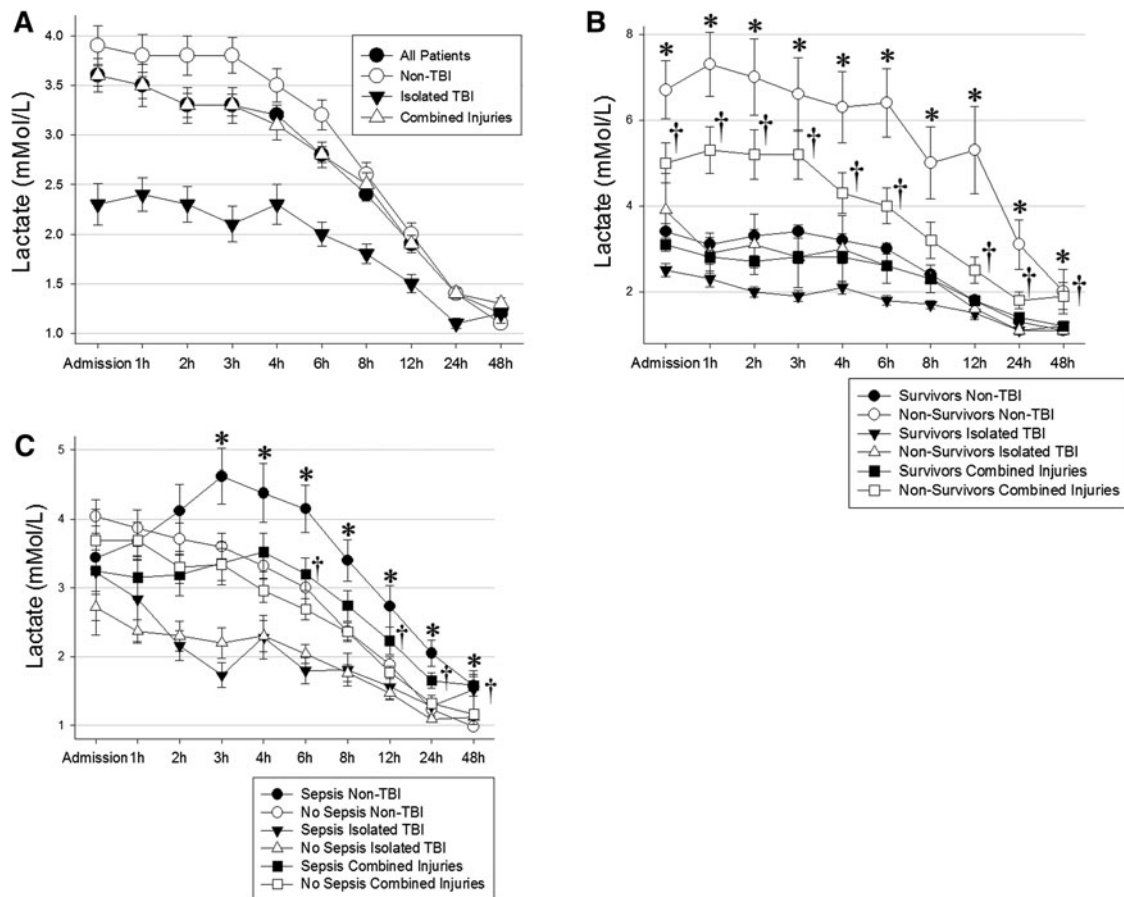
#### Serial lactate values

Figure 1a shows serial lactate values according to the different subgroups. Patients without TBI show, on average, the highest lactate values, whereas the lowest values were seen in patients with isolated TBI. Comparing survivors and non-survivors of the three subgroups, non-survivors of the non-TBI group showed the highest lactate values over time, which was statistically significant at every time point measured. The same trend was observed in patients with combined injuries, despite slightly lower lactate levels. Only non-survivors of the isolated TBI group did not differ with respect to lactate values over time (Fig. 1b).

Using sepsis as an endpoint, both the group of patients without TBI and the group with combined injuries showed higher mean lactate values over time, which became significant after 3 h [non-TBI patients ( $4.6 \pm 0.4$  vs.  $3.6 \pm 0.2$  mmol/L,  $p = 0.005$ )] and 6 h in patients with combined injuries. Patients with isolated TBI showed no differences in lactate values between patients who later develop sepsis and those who do not (Fig. 1c).

#### Serial base excess

Figure 2a depicts the mean serial BE values. The lowest BE values were recorded in patients without TBI in the first 6–8 h. Similar to the course of lactate, non-survivors of patients without TBI exhibited the lowest BE 1 h after admission ( $-13.8 \pm 1.5$  vs.  $-5.7 \pm 0.4$  mmol/L,  $p < 0.001$ ), with a clear difference until 12 h after admission (all  $p < 0.01$ , Fig. 2b). Patients with combined injuries had a comparable



**Fig. 1** **a** Serial lactate values in the whole collective. **b** Serial lactate values in survivors and non-survivors. **c** Serial lactate values in septic and non-septic patients. Overview of the mean lactate course over time in the three subgroups. The *error bars* indicate the standard error

of the mean (SEM). \* $p \leq 0.05$  comparing survivors and non-survivors of the non-TBI group; † $p \leq 0.05$  comparing survivors and non-survivors of the combined injuries group

curve to non-TBI patients at a higher mean BE, but with significant differences only between admission and 3 h (all  $p \leq 0.011$ ), and again at 24 and 48 h. In the isolated TBI group, survivors and non-survivors showed almost identical BE values at the time of admission.

Comparing the course of BE in septic and non-septic patients (Fig. 2c), differences were less evident. Patients without TBI who later become septic showed greater BE at 2, 3, and 24 h after admission (all  $p \leq 0.033$ ). The same was true for patients with combined injuries at 2 and 48 h ( $p = 0.039$  and  $0.025$ ). Again, BE values in isolated TBI patients did not differ in septic and non-septic patients (Fig. 2c).

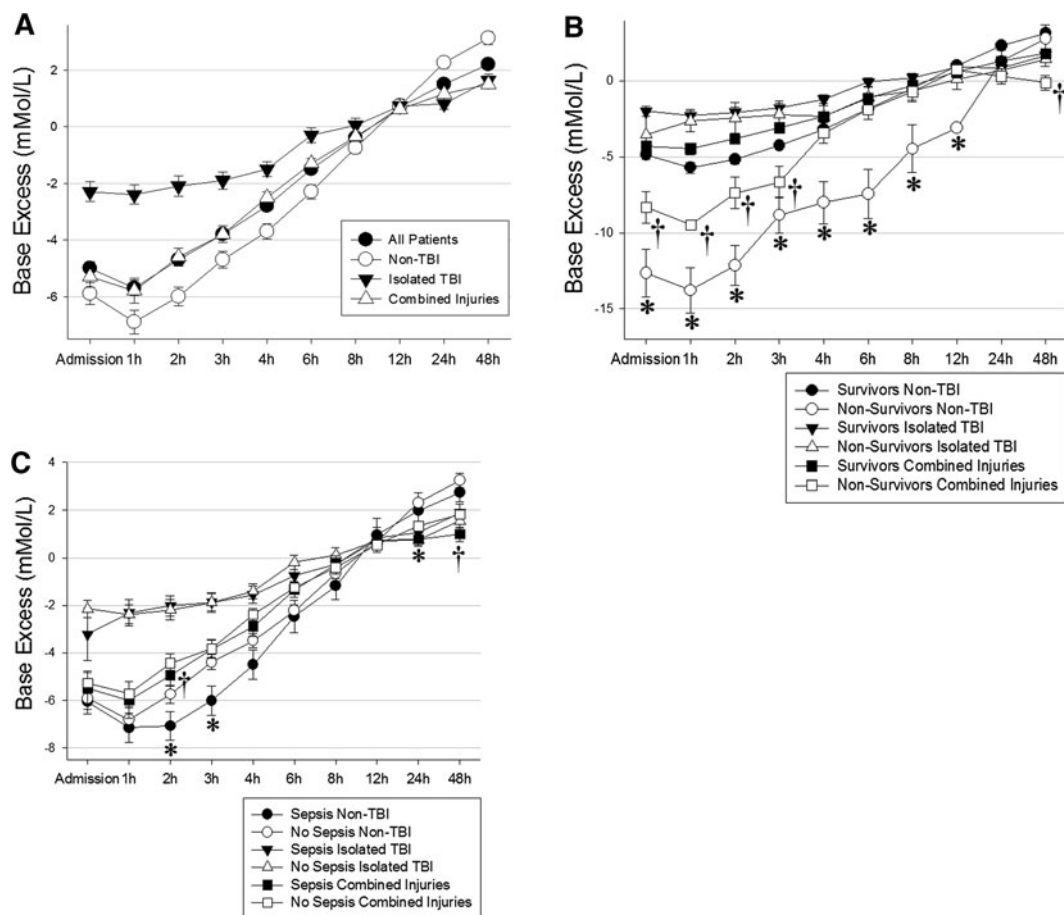
#### Lactate clearance

In the entire patient cohort, mortality increased from 19.1 % in patients that were unable to clear lactate below 2.5 mmol/L within 6 h (lactate always above 2.5) to a

mortality of 31 % in patients unable to clear below this threshold value within 48 h. In general, lactate clearance was impaired in non-survivors as compared to survivors. In the three subgroups, a distinction between survivors and non-survivors using lactate clearance below 2.5 mmol/L was only significant in patients without TBI. In patients with isolated TBI as well as in those with combined injuries, no significant differences were recorded between survivors and non-survivors.

When using sepsis as an endpoint, any patients unable to clear their lactate below 2.5 mmol/L within 6 h were more likely to become septic than those who were ( $p < 0.01$ ). Non-TBI patients with lactate levels remaining above 2.5 mmol/L 8 h after admission subsequently became septic in 33 % of cases ( $p < 0.05$ ). Patients with combined injuries and lactate above 2.5 mmol/L showed sepsis rates of 37.1 % (unable to clear within 6 h,  $p = 0.048$ ), 60 % (unable to clear within 24 h,  $p = 0.015$ ), and 66.7 % (unable to clear within 48 h,  $p = 0.016$ ).





**Fig. 2** **a** Serial base excess (BE) in the whole collective. **b** Serial BE in survivors and non-survivors. **c** Serial BE in septic and non-septic patients. Overview of the mean BE course over time in the whole collective and the three subgroups. The error bars indicate the SEM.

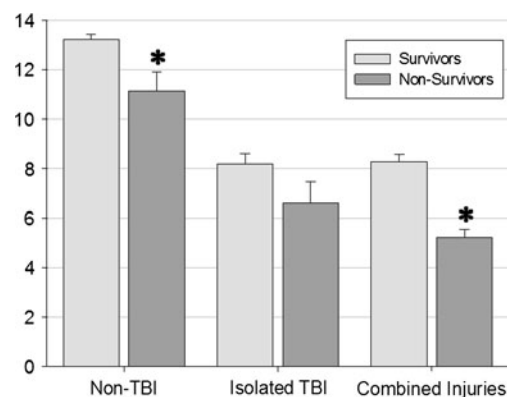
\* $p \leq 0.05$  comparing survivors and non-survivors of the non-TBI group;  $^{\dagger}p \leq 0.05$  comparing survivors and non-survivors of the combined injuries group

### Glasgow Coma Scale

Figure 3 depicts the mean initial GCS values in survivors and non-survivors of the entire collective. Non-survivors showed significantly lower GCS scores than survivors ( $10.4 \pm 0.2$  in survivors vs.  $7.3 \pm 0.4$  in non-survivors,  $p < 0.001$ ). In patients without TBI and those with combined injuries, survivors had significantly higher GCS scores [non-TBI:  $13.2 \pm 0.2$  (survivors) vs.  $11.1 \pm 0.8$  (non-survivors),  $p = 0.019$ ; combined injuries:  $8.3 \pm 0.3$  (survivors) vs.  $5.2 \pm 0.4$  (non-survivors),  $p < 0.001$ ]. In the smaller group of patients with isolated TBI, the difference in the initial GCS did not reach statistical significance ( $8.2 \pm 0.4$  in survivors vs.  $6.6 \pm 0.9$  in non-survivors,  $p = 0.064$ ).

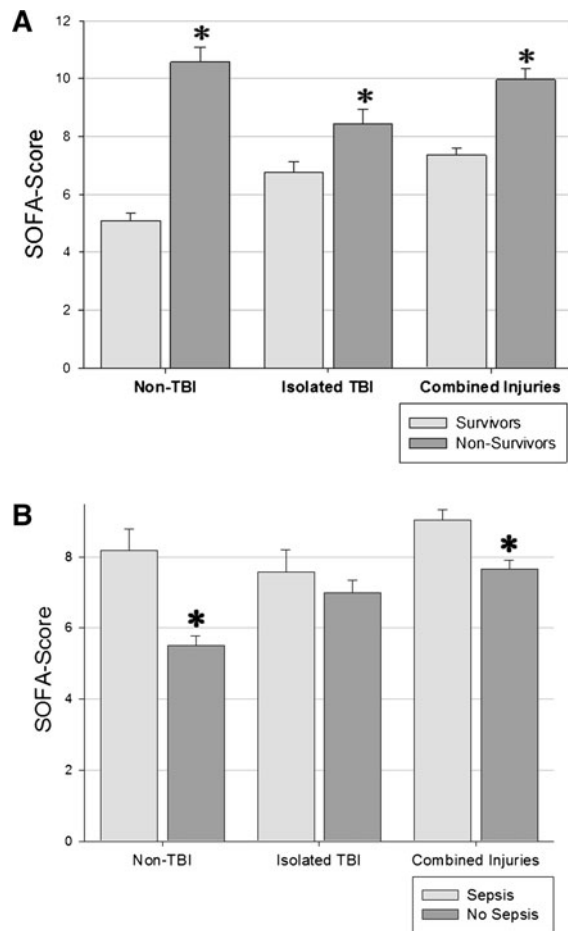
### Sequential Organ Failure Assessment

Figure 4a shows admission SOFA scores in surviving and non-surviving patients. Non-survivors showed higher SOFA scores than survivors in all subgroups (non-TBI/combined



**Fig. 3** Initial Glasgow Coma Scale (GCS) score in survivors and non-survivors. Depicted are the mean  $\pm$  SEM GCS values for each patient subgroup: non-TBI, isolated TBI, and combined injuries. \* $p \leq 0.05$

injury groups:  $p < 0.001$ , isolated TBI:  $p = 0.023$ ). In contrast to the other parameters in this study, the SOFA score was the only parameter able to distinguish non-survivors



**Fig. 4** Admission SOFA score. Overview of admission Sequential Organ Failure Assessment (SOFA) score with respect to outcome. **a** Mortality. **b** Sepsis. The error bars indicate the SEM. \* $p \leq 0.05$

from survivors in the subgroup of patients with isolated TBI. Furthermore, admission SOFA scores were higher in patients who, at some point, become septic compared to those who did not (Fig. 4b), which was especially evident in patients who did not sustain TBI (all  $p \leq 0.005$ ).

Length of mechanical ventilation, and lengths of ICU and hospital stay

The lengths of hospital and ICU stay, and the length of mechanical ventilation for each group are shown in Table 1. Notably, patients without TBI required the shortest time of mechanical ventilation and ICU stay, yet the longest hospital stay. The opposite was true for patients with isolated TBI, presumably due to early referral to specialized rehabilitation facilities.

Receiver operating characteristic analysis

The results of the ROC curve analysis are shown in Table 2 as the area under the curve (AUC) along with the 95 % CI,

as well as the designated time point and laboratory value. In summary, for the entire collective as well as for the subgroups, lactate showed the best predictive value for death at early time points. Using sepsis as an endpoint, the highest AUC values for lactate were recorded at later time points, i.e., 24 and 48 h (Table 2). The predictive values of BE, SOFA score, and GCS score were considerably lower.

Logistic regression analysis

In the whole collective, lactate at 6/8 h after admission was the only independent predictor for death as the outcome [odds ratio (OR) 1.41, 95 % CI 1.24–1.6]. No independent predictor for sepsis in the whole collective was found. Analysis of the subgroups did not reveal a useful independent predictor for either death or sepsis. Based on the findings of the ROC curve analysis, we were unable to find additional significance for any combination of the parameters tested.

## Discussion

Predictors of outcome are meant to help clinicians appreciate which trauma patient may be at risk of septic infections, organ dysfunction, and increased mortality or, alternatively, which patient may be fit for secondary operations or ICU discharge. Due to the nature of trauma, most previous studies were conducted in heterogeneous study populations, making any assertions of such parameters on specific injuries or patient subgroups difficult. The aim of our present study was to compare the prognostic value of frequently used outcome parameters in different patient subgroups to define the strengths and weaknesses of these parameters.

Lactate is a commonly used predictor of outcome in trauma and general surgery [14, 15], and has been shown to be a predictor of MOF in septic patients [16]. Our results support these findings, in that lactate was the best predictor of death and septic complications in the entire collective and any subgroup analyzed. Similarly, Aslar et al. [17] have shown that lactate is a predictor of death in their study on 64 patients with torso injuries comparable to our non-TBI group, and that lactate correlates with APACHE II scores following such injuries.

With respect to isolated TBI, the data about the elevation of serum lactate in patients with isolated head injury and their prognostic value are conflicting [18, 19]. In our study, lactate is the parameter with the highest AUC in the ROC curve analysis for death and sepsis in patients with isolated TBI, although it was not an independent predictor for either endpoint. An explanation for this may be that elevated lactate following fatal TBI is caused by



**Table 2** Results of the receiver operating characteristic (ROC) curve analysis for arterial lactate

	Exitus [AUC (95 % CI)]		Sepsis [AUC (95 % CI)]	
	Admission	Time point with highest AUC	Admission	Time point with highest AUC
All patients	0.67 (0.61–0.74)	1/2 h: 0.71 (0.64–0.78)	0.5 (0.44–0.56)	48 h: 0.7 (0.65–0.75)
Non-TBI	0.63 (0.52–0.73)	1/2 h: 0.66 (0.55–0.77)	0.46 (0.35–0.57)	24 h: 0.65 (0.54–0.75)
Isolated TBI	0.65 (0.51–0.78)	6/8 h: 0.75 (0.63–0.87)	0.49 (0.35–0.64)	24 h: 0.71 (0.59–0.83)
Combined injuries	0.74 (0.65–0.83)	1/2 h: 0.77 (0.67–0.87)	0.54 (0.45–0.63)	48 h: 0.71 (0.59–0.83)

Data are listed with designation of the appropriate laboratory value and time point, as well as the area under the curve with 95 % confidence interval

AUC area under the curve, TBI traumatic brain injuries

deteriorating peripheral tissue oxygenation late after trauma, but other factors may play a role. A potential variance of lactate by intravenous fluids is a frequently discussed, even though Jackson et al. [20] showed in 1997 that Ringer's lactate does not affect the serum levels in ICU patients as long as the sample was not drawn from the intravenous line arm.

Our results contrast those of Zehtabchi et al. [19], who found no correlation between the severity of brain injury and arterial lactate, which may be due to the fact that their study also included patients without intracranial lesions on CT. Cureton et al. [18] did find a correlation between the severity of TBI and admission lactate in their study on 555 TBI patients. Because of better survival in patients with lactate >5 mmol/L, the authors even suggested a protective effect following brain injury. We did not observe such an effect, which may be either be due to more severe head injuries in our patients or as a result of occult hypoperfusion, a known risk factor for subsequent infectious complications [21, 22].

In our study, lactate also serves as a predictor of septic complications, where it showed the highest associations at 24 and 48 h after admission. This is true for all three subgroups, and underlines the need for ongoing lactate monitoring for the early recognition of under-resuscitated patients or those developing complications. However, despite the fact that lactate was the best prognostic factor in this study, it is important to consider that the AUC values were in an area of fair accuracy, or slightly below 0.7.

BE is considered as a useful marker of increased mortality, transfusion requirements, or significant abdominal injury [23–26]. In our study, serial BE provided a picture similar to lactate in the first 48 h, especially in patients without TBI. However, the ROC curve and multivariate analysis found BE to be inferior in predicting mortality or sepsis in our patients. Correspondingly, Mikulaschek et al. [27] demonstrated the superiority of lactate to BE and showed that no direct correlation exists between lactate and BE. Our results support these findings, and we see no

specific additional value in routine BE measurements over lactate.

The GCS was originally developed for postoperative surveillance after neurosurgery, before it was used in TBI [28]. Kennedy et al. [29] showed that the GCS score correlates with outcome following gunshot head injuries. The GCS has later become a standard score and correlates well with findings in head CT scans as well as with clinical outcome [30]. In our study, though, we cannot support the GCS as an overall predictor for mortality. Even following isolated TBI, the GCS was not useful to predict fatal outcome. Indeed, several recent studies could demonstrate good survival and satisfactory outcome, even in patients with an admission GCS score of 3 [31–33]. In severe TBI, pupil reaction on admission has been shown to be a potentially more valid predictor of outcome [31–33].

In our study, non-survivors with additional injuries showed lower initial GCS values than non-survivors with isolated TBI. We assume this to be due to an influence of non-head injuries on the GCS score. Hemorrhagic shock, for instance, seems to impair brain function in an uncontrolled way, since non-survivors without TBI show lower initial GCS scores than survivors. Demetriades et al. [34] have provided a model based on the admission GCS score, head AIS, mechanism of injury, and patient age with superior performance in predicting fatal outcome compared to the initial GCS score alone (overall 94.2 % correct classification rate). In conclusion, low GCS score does not appear to be a good predictor for fatal outcome, and should likely not be used as a decision-making aid in patients with injuries other than isolated TBI.

The SOFA score as the final parameter of interest in this study has already been proven to be a reliable outcome parameter in trauma patients [10]. It was also shown to correlate with mortality from cancer, sepsis, and even stem cell transplantation [11, 35]. A key factor for its success is the incorporation of therapeutical information: in cardiovascular (CV) failure, for instance, the administration of catecholamines is accounted for, which may be the main

reason for its superior predictive value compared to the score by Peres Bota et al. [36].

In our study, admission SOFA scores showed significant differences between both survivors and non-survivors and between septic and non-septic patients (Fig. 4). However, the ROC curve analysis revealed inferior AUCs for death and sepsis as endpoints for all subgroups. Of note, in isolated TBI, the SOFA score was the only parameter which was significantly different between survivors and non-survivors (Fig. 4a). The limited predictive value in isolated TBI is probably based on two main factors. First, the assessment of GCS score in intubated patients leads to falsely lower GCS scores on admission. Secondly, patients with TBI often require CV support in order to maintain sufficient cerebral perfusion pressure, thereby, prohibiting a better differentiation of patients with CV failure due to compression of the brainstem.

A recent study found a correlation between lactate levels and SOFA score in 134 mixed ICU patients [37]. In this study, a relationship existed between both parameters during the early ICU stay, indicating a link between early resuscitation, as indicated by AUC measurements of lactate >2.0 mmol/L, and the prevention of organ failure, as assessed by SOFA scores. The authors concluded that hyperlactatemia may, indeed, be considered as a warning signal for subsequent organ failure.

The limitations of this study should be noted: major advances in resuscitation techniques and protocols have occurred during the study period of 11 years, which may add a bias to this analysis. Patients treated after 2006 have been deliberately excluded from this analysis, since trauma protocols, use of subspecialty consults, and database inclusion criteria have changed at the authors' institutions in 2007/2008. Despite being used as a marker of hypoperfusion since the early 1990s, the precise role of lactate in ICU patients is still being defined [37]. The findings of our study are derived from select subgroups of a retrospective exploratory analysis, and generalizations to other patient subsets may not be made. Yet, in summary, our study indicates that lactate may be the most valid prognostic laboratory parameter in both head-injured and non-head-injured patients. Its use may help identify patients in need of early therapeutic intervention to avert adverse outcome resulting from systemic or local hypoperfusion.

**Conflict of interest** None.

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